PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 58040-A-PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/12536	International filing date *(day/month/year)* 04 MAY 2000	Priority date *(day/month/year)* 04 MAY 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 38/16 and US Cl.: 514/2, 21		
Applicant THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☐ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
04 DECEMBER 2000	17 SEPTEMBER 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Dorothea Lawrence for JEAN C. WITZ Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/12536

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-34 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 35-37 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-9 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/12536

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-21	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	1-21	YES
	Claims	NONE	NO
Industrial Applicability (IA)	Claims	1-21	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1-21 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the use of a gp130 receptor ligand and a growth factor to induce mesenchymal precursor cells to differentiate into kidney epithelia.

---------- NEW CITATIONS ----------
NONE

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claims 1-21 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

The specification indicates that a combination of a gp130 receptor ligand, specifically LIF, in combination with a growth factor, most specifically TIMP, resulted in epithelialization of metanephric mesenchyme and formation of tubules and nephrogenesis in vitro. This has confirmed the state of the art that LIF alone has little effect in vitro on growth or on ureteric-bud morphogenesis other than to stimulate the bifurcation process. The state of the art also acknowledges that renal mesangial cells both synthesize and react to LIF. LIF is not mitogenic for the mesangial cells. LIF is excreted in the urine of kidney transplant patients undergoing acute rejection but is not found in stable graft recipients. Transgenic mice that overexpress LIF develop mesangial proliferative glomerulonephritis. While numerous growth factors have some influence on kidney development, the state of the art indicates that the specification has shown a developmental effect on kidney mesangial cells of LIF combined with TIMP, such showing is insufficient to enable claims to in vivo treatments of kidney disease and failure. It remains unpredictable as to the interactions of the growth factors with the extant kidney tissue as well as the response of the transplanted primoridal kidney tissue when exposed to the in vivo biochemistry and physiology. This is particularly true of claim 4 and those claim that depend from same as there is no showing or suggestion of is supposed to occur when the LIF and the TIMP are administered. It would appear that the etiologies of the different types and causes of the kidney failure would be expected to have an effect upon how that kidney failure is treated. Therefore the cited claims are not enabled by the specification.